Esophageal motility in small animals

Kook, Peter H

ESOPHAGEAL MOTILITY IN SMALL ANIMALS

Dr. med. vet. Peter Hendrik Kook, Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland

Anatomy and physiology: The esophagus is a hollow muscular tube transporting liquid and ingesta to the stomach. It consists of the upper esophageal sphincter (UES), the tubular esophagus, and the lower esophageal sphincter (LES). The entire length of the canine esophagus is composed of striated muscle (the smooth lamina muscularis mucosae does not contribute to peristalsis), whereas the distal one third of the feline esophagus is composed of smooth muscle. Although the canine tubular esophagus is composed of striated muscle, it should be noted that most of the canine LES consists of smooth muscle.[1] The lining of the esophagus is a robust stratified squamous epithelium which terminates abruptly at the point of entry into the stomach into a simple columnar lining.

Swallowing consists of a series of sequential well-coordinated events that transport food and liquids from the oral cavity to the stomach. This process can be divided into three major phases: oropharyngeal, esophageal and gastroesophageal.

Unlike most other parts of the gastrointestinal tract, coordinated motor function depends on an extrinsic nervous system; the vagus nerve and associated branches innervate the esophagus. The neural coordination contains somatic motor nerves from the brain stem nucleus ambiguous to the esophageal striated muscle, autonomic nerves to the esophageal smooth muscle, and general visceral afferent nerves from the esophageal sensory receptors. In the pharyngeal phase of swallowing, bolus movement through the pharynx is accomplished by sequential contractions of pharyngeal muscles initiated by the stimulation of sensory receptors. The corresponding nerve fibres are in the maxillary branch of CN V, in CN IX, and in the cranial laryngeal nerve. These afferent pathways carry the information from peripheral receptors to the brain stem, evoking contraction of the buccal, tongue, pharyngeal, and esophageal muscles and thereby propelling the food bolus aborally. Particular sensory pattern determine which pharyngeal motor responses will be evoked. Generally, solid boluses are more effective than liquids in stimulating pharyngeal receptors to initiating swallowing, and in health multiple swallowing attempts may sometimes be necessary to stimulate deglutition of water. This explains why increasing bolus viscosity of liquids is used as a basic therapeutic strategy to protect patients with oropharyngeal dysphagia from aspiration.

The esophageal phase of swallowing begins with relaxation of the UES, thus moving the food bolus into the proximal esophagus. The first peristaltic wave initiated in the pharynx carries the bolus further aborally (primary peristalsis). If the primary peristalsis is insufficient to propel the bolus into the stomach, a second peristaltic wave is generated by esophageal distension-sensitive receptors cranial to the bolus that complete bolus transport.[2] Any interference with this sensory re-inforcement of the swallowing reflex may result in disordered esophageal motor activity, illustrating why esophageal inflammation in itself may also cause esophageal hypomotility. For instance, in cats, experimentally induced esophagitis decreases esophageal peristalsis, reduces LES pressure, and diminishes esophageal clearance. These changes were reversible with healing of the esophagus.[3-5] The LES finally relaxes in advance of tubular esophageal pressures and contracts again after the bolus has passed, thereby preventing reflux of gastric contents. The LES resting pressure is maintained by two excitatory neural influences (vagal cholinergic, as well as non-vagal mechanisms mediated by alpha-adrenergic and cholinergic receptors). Baseline pressures can vary in awake dogs between 14 and 45 mm Hg (median ≈ 30 mm Hg)[6,7] which is considerably higher compared to humans.

Age-related changes in esophageal function: Age-related delays in esophageal maturation must be considered when evaluating young pets presenting for apparent swallowing abnormalities.[2] More recently, Bexfield et al. have described the phenomenon of delayed esophageal maturation in young dogs: Fluoroscopic evidence of esophageal dysmotility, either segmentally or globally, was present in clinically affected young dogs (median 9 months) presenting for regurgitation or anorexia, as well as in some clinically normal dogs (median 11 months).[8] None of the described dogs had radiographic evidence of esophageal dilation. Subsequent improvement of esophageal motility was noted fluoroscopically in the majority of clinically affected and asymptomatic dogs. Terrier dogs predominated in that study, nonterrier breeds included a Labrador Retriever and a Rottweiler. Interestingly, in the "asymptomatic" clinically normal control group abnormal videofluoroscopic swallowing studies were only observed in terrier dogs.[8]

While **primary esophageal motility disorders** occurring in the absence of an identifiable cause such as achalasia, diffuse esophageal spasm, nutcracker esophagus or the hypertensive lower esophageal sphincter have been clearly identified in humans,[9] primary esophageal motility abnormalities have yet to be uncovered in small animals. For instance achalasia - the most well-defined esophageal motor disorder in people - has only very recently been documented in dogs.[10] The major problem seems to be the lacking agreement on corresponding clinical signs relevant to esophageal dysmotility. While a human patient subjectively experiences a symptom (such as retrosternal pain or heartburn) and reports it to the examining physician, our patients cannot speak and it is intrinsically difficult to sense and assess less obvious signs during anamnesis or examination.

At present the concept of "esophageal motility problems" in small animal medicine mostly focuses on a variety of disease conditions that have been reported to affect esophageal motility. Neuromuscular diseases (inflammatory, immune-mediated, infectious, and degenerative/idiopathic) account for the largest group, followed by less common entities such as endocrine disease (hypoadrenocorticism, hypothyroidism), toxicities (lead, thallium), acquired brain stem disease, as well as congenital central nervous or peripheral dysfunctions. As stated above, clinical signs of esophageal dysmotility may not be readily apparent, can be overshadowed by the underlying primary disease process, and can range from anorexia to regurgitation or dysphagia. Depending on the causative disease process and magnitude of additional esophageal inflammation, vomitus may also be seen.

Evaluation of esophageal motility – available diagnostic procedures
In veterinary medicine comparative studies evaluating the pros and cons of different diagnostic procedures for the assessment of esophageal function are lacking. Plain (+/- contrast) thoracic radiography are often used as an initial step to screen for esophageal dilation, possible intraesophageal fluid/foreign material, esophageal masses, and possible associated pulmonary changes. However radiographs (plain or contrast) cannot assess esophageal function. Barium contrast videofluoroscopy may help defining normal pharyngeal, UES, esophageal and LES anatomy and has been used to evaluate oropharyngeal dysphagias. It has been suggested that performing frame-by-frame analysis of recorded fluoroscopic studies could provide quantitative measures of swallowing function in cases of asynchronous UES opening, and the normal timing of the swallowing act has been reported.[11] However it should be noted that this imaging modality can only detect gross abnormalities of pharyngeoesophageal function. The procedure is subjective and more subtle disorders of the swallowing reflex can be difficult to detect. Also feeding a consistent barium-soaked bolus size to the dogs is often impossible, and many patients are unreceptive to feeding necessitating force-feeding which can result in unnatural feeding activity. Furthermore patient motion during chewing and swallowing often make adequate visualization of the pharyngeal and esophageal regions difficult.[11] The existing criteria for the fluoroscopic assessment of tubular esophageal function are mostly descriptive, and in parts conflicting. For example esophageal contrast retained for several seconds without stimulation of a secondary peristaltic wave has been considered abnormal by some authors,[8,12] while fluoroscopic evaluation of the passage of oral medication when given as a wet swallow in healthy cats indicates that intraesophageal contents may also be retained longer.[13]

Esophageal manometry allows the depiction of pressure profiles generated by esophageal peristalsis and provides clinically relevant information on esophageal motor function. Conventional manometry involves the use of catheters with a few widely spaced channels that are continuously perfused with water. Differences in the resistance to water flow among the manometric channels are measured by pressure sensors and then converted to an electrical signal, and recordings are interpreted as line tracings. Because of the small number of channels and the wide gaps between those channels, a time-consuming pull-through technique is usually needed. Use of an increased number of pressure sensors on the catheter and creation of spatiotemporal contour plots for data display have provided a new technique: **High-resolution manometry (HRM)**.
HRM has become the criterion-referenced standard for the evaluation of esophageal function in humans. Most importantly the dynamic interaction of the UES, tubular esophagus, and LES during swallowing can be evaluated concurrently, which facilitates detection of disorders in this complex functional system.[10]
Furthermore, the soft catheter material improves patient comfort during its nasal insertion. HRM examinations are performed with the patient in a sitting position. The HRM catheter is lubricated with a 2% lidocaine gel, passed intranasally, and positioned to record the entire esophagus from the pharynx to the stomach. Real-time pressure monitoring is used to ensure accurate catheter placement. Three or 4 pressure sensors are positioned intragastrically to enable measurement of gastric reference pressure and to rule out artifacts of the esophagogastric junction caused by breathing-related movements.[6]
In humans, HRM constitutes the gold standard for evaluating esophageal function. Utilizing color-coded pressure topography, HRM quickly enables the examiner to obtain an impression of the integrity of the whole swallowing act. The whole esophagus can be visualized at the same time, from the pharynx to the stomach (Fig.1). We have recently evaluated the feasibility of this noninvasive technique in awake healthy dogs.[6] Because intranasal insertion of this costly catheter may be problematic in uncooperative awake patients, we also assessed potential effects of a standard sedation on manometric data.[6] We found that sedation may minimally influence results of some variables, but an overall assessment of swallowing still seemed possible. At this time, the clinical relevance of the observed differences (awake versus sedated) is unclear. Also it is not clear to what extent sedation would also affect HRM analysis in dogs with esophageal motility disorders. Therefore, the primary goal should always be to examine esophageal function of a patient in an awake state, and sedation should be reserved for uncooperative dogs.
Because HRM enables a non-invasive evaluation of esophageal function in dogs, its routine clinical application will greatly facilitate investigations whether primary esophageal motility disorders also play a role in veterinary medicine. One example would be achalasia - a disease of unknown cause associated with functional loss of myenteric plexus ganglion cells in the distal esophagus. It is the most common esophageal motility disorder in people where it is characterized by the absence of distal esophageal peristalsis and inadequate LES relaxation.[14] The degenerative process appears to involve preferentially the nitric oxide producing inhibitory neurons that affect relaxation of esophageal smooth muscle. In people, achalasia can be subtyped into 3 groups based on manometric esophageal body pressure profiles. Type 1 is the complete absence of peristaltic contractile activity and minimal pressurization. Type 2 denotes the absence of peristaltic contractile activity with esophageal pressurization, and type 3 is characterized through spastic esophageal contractions.[14] We could recently document for the first time a case of canine achalasia similar to human type 2 achalasia in a myasthenic pug.[10] The key clinical sign suggestive of an underlying esophageal motor disorder in that case was the patients' unexplained anorexia. In humans with type 2 achalasia, it is known that the esophageal pressurization action is perceived as very painful, it is usually described as a concurrent chest pain. Most probably the same holds true for dogs, and refusal to eat in our case was due to accompanying pain during the act of swallowing.[10] Future

implementation of HRM in the work-up of dogs presenting with unexplained clinical signs possibly suspicious for esophageal motor disease will help determining in what way primary esophageal motility disorders also play a role in our patients.

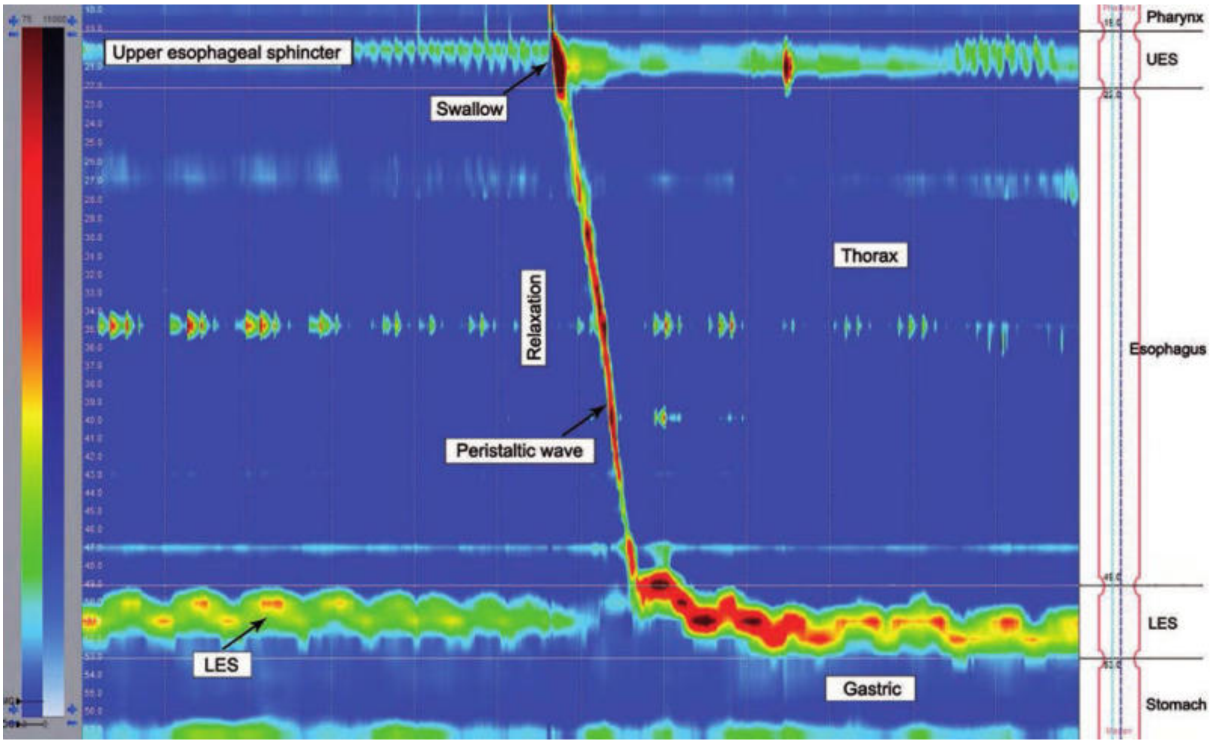

Fig.1: Representative topographic display of the physiologic swallow pressure profile from the pharynx to stomach in a healthy dog recorded by use of an HRM catheter. The examination was performed with a 40-channel solid-state probe with 10-mm spacing between adjacent pressure sensors. The colors reflect the intensity of the pressures; red represents high pressure and blue represents low pressure (color scale on the left side). The UES and LES are clearly detectable as high-pressure zones, and the tubular esophagus extends between the 2 sphincters. A relaxation of both sphincters following a swallow is visible. The scale on
the right side indicates the position of the catheter in the body (recording speed, 60 s/frame).[7]

1. Mann CV, Shorter RG. Structure of the canine esophagus and its sphincters J Surg Res 1964;4:160–1631
2. Guilford WG, Strombeck DR. Diseases of swallowing. In: Guilford WG, Center SA, Strombeck DR, Williams DA, Meyer DJ, eds. Strombeck's Small Animal Gastroenterology, 3rd ed. Philadelphia, PA: WB Saunders; 1996:211-238
3. Eastwood GL, Castell DO, Higgs RH. Experimental esophagitis in cats impairs lower esophageal sphincter pressure. Gastroenterology 1975;69:146-153
4. Liebermann-Meffert D, Klaus D, Vosmeer S, Allgöwer M. Effect of intraesophageal bile and acid (HCl) perfusion on the action of the lower esophageal sphincter. Scand J Gastroenterol Suppl 1984;(92):237-241
5. Zhang X, Geboes K, Depoortere I, Tack J, Janssens J, Sifrim D. Effect of repeated cycles of acute esophagitis and healing on esophageal peristalsis, tone, and length. Am J Physiol Gastrointest Liver Physiol 2005;288:G1339–G1346
6. Kempf J, Heinrich H, Reusch CE, Kook PH. Evaluation of esophageal high-resolution manometry in awake and sedated dogs. Am J Vet Res 2013;74(6):895-900
7. Kempf J, Lewis F, Reusch CE, Kook PH. High-resolution manometric evaluation of the effects of cisapride and metoclopramide hydrochloride administered orally on lower esophageal sphincter pressure in awake dogs. Am J Vet Res. 2014;75(4):361-366
8. Bexfield NH, Watson PJ, Herrtage ME. Esophageal dysmotility in young dogs. J Vet Intern Med 2006;20(6):1314-1318
9. Patti MG, Herbella FA. Achalasia and other esophageal motility disorders. J Gastrointest Surg 2011;15(5):703-707
10. Kempf J, Beckmann K, Kook PH. Achalasia-like disease with esophageal pressurization in a myasthenic dog. J Vet Intern Med 2014;28(2):661-665
11. Pollard RE, Marks SL, Davidson A, Hornof WJ. Quantitative videofluoroscopic evaluation of pharyngeal function in the dog. Vet Radiol Ultrasound 2000;41(5):409-412
12. Stickle R, Sparschu G, Love N, Walshaw R. Radiographic evaluation of esophageal function in Chinese Shar Pei pups. J Am Vet Med Assoc 1992;201(1):81-84

13. Westfall DS, Twedt DC, Steyn PF, Oberhauser EB, VanCleave JW. Evaluation of esophageal transit of tablets and capsules in 30 cats. J Vet Intern Med 2001;15(5):467-470
14 Pandolfino JE, Kahrilas PJ. Presentation, diagnosis, and management of achalasia. Clin Gastroenterol Hepatol 2013;11(8):887-897¨